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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/702,134	10/31/2000	Andrey A. Boukharov	04983.0201.00US00/38-21(5	8935

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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	**PAPER NUMBER**
1634	

MAIL DATE	DELIVERY MODE
11/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/702,134	BOUKHAROV ET AL.	
	Examiner	Art Unit	
	JEANINE A. GOLDBERG	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 8-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1 and 23-25* is/are allowed.

6)☒ Claim(s) *8-11,13-16 and 18-21* is/are rejected.

7)☒ Claim(s) *12,17 and 22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed August 28, 2008 and June 5, 2008. Currently, claims 1, 8-25 are pending.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. Any objections and rejections not reiterated below are hereby withdrawn.

a. The Written Description rejection has been withdrawn in light of the Written Description Guidelines.

b. The 101 rejection previously of record was withdrawn in view of the new evidence provided by the examiner.

The examiner carefully considered the arguments that applicants believed SEQ ID NO: 7212 comprises a Gibberellin based upon homology and Table 2 at positions 29572-30174. The examiner performed extensive search of encoded proteins of Gibberellin C-20 and found over 13 additional Gibberellin known in the art at the time the invention was made. An alignment of the known Gibberellin is provided in Kang et al. (Plant Physiology, Vol. 121, page 373-382, October 1999). A comparison of the encoded protein from positions 28575-30173 of SEQ ID NO: 7212 with the prior art illustrates the conserved regions of the enzyme. The sequences do differ in the region of amino acid 106-116. The amino acid from SEQ ID NO: 7212 would produce a protein comprising RAQRRAGESCGY. The amino acid from the art would produce RRSGARGRTAY. The regions that differ do not appear to be within critical domains, according to Kang. The R, G, GY appear to be conserved over the art, see Kang. Similarly, Perez-Flores (J. of Experimental Botany, Vol. 54, No. 390, pages 2071-2079,

September 2003) aligns 7 Gibberellin molecules and the region where the variations between SEQ ID NO: 7212 exist do not appear to be in critical regions. Therefore, given the high degree of similarly between SEQ ID NO: 7212 and Genbank U50333, a Oryza sativa gibberellin C-20 oxidase mRNA and the alignments taught in the art to demonstrate the encoded protein does not differ in regions which would likely affect the activity of the enzyme, it is more likely than not that positions 28575-30173 of SEQ ID NO: 7212 encodes a gibberellin C-20 oxidase. Thus, the entire SEQ ID NO: 7212 would have at least one use to meet the utility requirement under 101.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 8-11, 13-16, 18-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of

direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

The claims are drawn to nucleic acid molecules sharing between 90-100% identity with SEQ ID NO: 7212.

The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

An alignment of the known Gibberellin is provided in Kang et al. (Plant Physiology, Vol. 121, page 373-382, October 1999).

Similarly, Perez-Flores (J. of Experimental Botany, Vol. 54, No. 390, pages 2071-2079, September 2003) aligns 7 Gibberellin molecules.

Guidance in the Specification.

The specification provides no evidence that variation up to 90% over SEQ ID NO: 7212 would maintain the use of gibberelin C-20 oxidase. The specification teaches SEQ ID NO: 7212. The specification provides, in Table 2, a very basic outline of the possible components of SEQ ID NO: 7212. The majority of the regions identified are not characterized. From position 28572-30174, Table 2 suggests the region is

"probable gibberellin C-20 oxidase". The specification fails to provide any guidance regarding molecules that have variation.

A nucleic acid with 90% identity with SEQ ID NO: 7212 would be permitted to have 6,900 differences over the sequence. A nucleic acid with 99% identity would be permitted to have 690 differences over the sequence.

The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied to enable the skilled artisan to use the claimed invention. The teachings of the specification and of the prior art do not enable one skilled in the art to use molecules sharing between 90-99% sequence identity with SEQ ID NO: 7212. Thus, the claims as written encompass allelic and splice variants SEQ ID NO: 7212 and fragments thereof, naturally and non-naturally occurring mutants of these sequence, variants isolated from other organisms, etc. In the approximately 69,000 bases of SEQ ID NO: 7212, a sequence which is 90% identical would encompass a sequence with 6,900 differences. The specification has not disclosed a biological function for the large genus of molecules encompassed by the claims, or otherwise provided guidance with respect to how such molecules may be used.

With respect to the claims requiring percentage identity, it would be unpredictable for the skilled artisan to determine how to use the nucleic acid sequence which shares homology with the claimed sequence. The response asserts that SEQ ID NO: 7212 comprises known nucleic acids which encode proteins, however, in the event that the variation exists in these regions, the nucleic acid would not share structure with the asserted use. For example, the region of 28575-30173 of SEQ ID NO: 72 upon which applicant relies up for utility is only 1571 nucleotides in length. In the event that the variation provided by the claims existed in the region which applicants provide is the useful part, the skilled artisan would be unable to use the claimed invention. For example, if the 1571 nucleotides of the gibberellin C-20 oxidase were altered, the nucleic acid would be unable to function as gibberellin C-20 oxidase. Thus, the nucleic acid of the claims would fail to be useful as a gibberellin C-20 oxidase. The skilled artisan would be required to perform unpredictable and undue experimentation to determine how to use nucleic acids which share only a percent identity with the claimed nucleic acid. With respect to 99% specifically. 99% permits up to 690 variations in the sequence of SEQ ID NO: 7212. This would permit changes in half of the residues of the gibberellin C-20 oxidase including those residues that materially affect the function of the enzyme. It would require further experimentation and trial and error research to determine how to use the sequences which are similar to those provided by SEQ ID NO: 7212.

Accordingly, while one of skill in the art could conduct further experimentation aimed at, e.g., identifying a particular function for the molecules of the claims, such a

function is not presently known, and the outcome of such experimentation cannot be predicted. Thus, it would require undue experimentation to use the claimed invention. This would require significant inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art for determining the function of nucleic acids, it is unpredictable how to use sequences that differ at any number of locations and affection the function of the nucleic acid. Further, the prior art and the specification provides insufficient guidance to overcome the art recognized. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Response to Arguments

The response traverses the rejection. The response asserts one of ordinary skill in the art would have the ability to make nucleotide substitutions to SEQ ID NO: 7212 without undue experimentation. This argument has been reviewed but is not convincing. The examiner acknowledges one could make the variant nucleic acid molecules with up to 6900 differences from SEQ ID NO: 7212. However, the examiner does not believe that the skilled artisan would have known how to use the variant nucleic acid molecules without further unpredictable and undue experimentation. As stated previously, the region of 28572-30174 has a known function. In the event that this region was completely altered, the skilled artisan would have been required to determine how to use the nucleic acid molecule.

The response argues that the examiner has identified a critical region of 28575-30173 of SEQ ID NO: 7212 which encodes a gibberellin C-20 oxidase and the skilled artisan would have the requisite skill to modify SEQ ID NO: 7212 in a manner commensurate in scope with the claims without undue experimentation. This argument has been reviewed but is not convincing. The scope of the claims encompass nucleic acid molecules in which ALL of the 1572 nucleotides between 28575-30173 are altered in addition to approximately 5,000 additional nucleotides are altered. The specification provides no guidance how to use these nucleic acids.

The response states that one skilled in the art would not change all 1571 nucleotides in the region of 28575-30173 with the expectation of maintatining functionality. This is exactly the examiners position. What is the skilled artisan going to use for when all 1571 nucleotides in the region 28575-30173 are altered since they will

not maintain the functionality of the protein. These nucleic acids are clearly encompassed within the instant claims.

Thus for the reasons above and those already of record, the rejection is maintained.

Objection

4. Claim 12 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

5. Claims 1, 23-25 are allowable.

6. Claims 12, 17, 22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

/Jeanine Goldberg/
Primary Examiner
November 5, 2008